

## Regular article

**Treatment of methamphetamine use disorders: an update**Richard A. Rawson, Ph.D.<sup>a,\*</sup>, Rachel Gonzales, M.P.H.<sup>a</sup>, Paul Brethen, M.A.<sup>b</sup><sup>a</sup>*UCLA Integrated Substance Abuse Programs (ISAP), 11050 Santa Monica Boulevard, Suite 100, Los Angeles, CA 90025, USA*<sup>b</sup>*Matrix Institute on Addictions, Los Angeles, CA 90025, USA*

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**Abstract**

Methamphetamine (MA) is a major public health and criminal justice problem in much of the Western and Midwestern US, and its use seems to be increasing east of the Mississippi River. MA use can produce significant psychiatric and medical consequences, including psychosis, dependence, overdose, and death. Cognitive behavioral therapy and contingency management are among the most promising approaches for treatment of MA abuse and dependence. A multisite study evaluating the Matrix Model of outpatient treatment will soon be completed to provide data on this manualized approach. An ambitious program of pharmacotherapy development research is currently being sponsored by the National Institute on Drug Abuse (NIDA) in geographic areas significantly affected by MA use. The development of treatments for MA-related problems is particularly critical for a number of user groups including MA users who experience persistent psychosis, pregnant women and women with children, gay and bisexual men, and MA users involved in the criminal justice system. © 2002 Elsevier Science Inc. All rights reserved.

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**1. Introduction**

Methamphetamine (MA) use has increased to epidemic proportions in some areas of the US and currently poses a significant public health threat (Anglin, Kalechstein, Maglione, Annon, & Fiorentine, 1997; National Institute of Justice, 1999; Pennell, 1999). MA use is the dominant drug problem in the Western and, more recently, Midwestern US, most severely impacting rural areas and numerous moderately-sized urban communities (Pennell, 1999). Recently, evidence of rapidly increasing MA production and use has been reported throughout Georgia and other areas of the rural South and among gay men in New York City (National Institute on Drug Abuse, 2001). There are a number of reasons to predict that MA-related problems may continue to escalate and spread (Rawson, Anglin, & Ling, 2002). According to a United Nations report, over 35 million individuals regularly use/abuse amphetamine/MA. In contrast, cocaine use is limited to

approximately 15 million worldwide (mostly North America) and heroin is used by fewer than 10 million (United Nations Office for Drug Control and Crime Prevention, 2000). In the US, what was once an almost exclusively Caucasian consumer base is expanding to Hispanic and Asian populations.

In addition to the large and expanding consumer market, it is easy to make MA and although access to the necessary precursor chemicals can be reduced, it is not likely the MA availability will decrease. Not only is MA likely to remain available, it is likely to remain inexpensive as well. MA effects are long lasting (10–12 hours) and MA users typically spend about 25% as much money for MA as that spent by cocaine users for cocaine (Rawson et al., 2000). Knowledge of how to manufacture MA has, over the past 10 years, been disseminated from a few “biker gang cooks” to two very important new groups. Creative “mom and pop chemists” can now download the formulas for MA from the Internet and produce small quantities for personal and associate use; and organized drug trafficking cartels have moved into the manufacturing of MA. With the addition of these two groups into the world of MA manufacture and supply, the availability of MA is likely to increase as new markets are created.

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At present, there are few signs to suggest that the MA epidemic of the 1990s will simply become an unpleasant memory (Rawson, Anglin, & Ling, 2002). For this reason, it is imperative that new knowledge be developed on the impact of MA on users and on new strategies for treating these individuals.

## 2. Effects of MA

“Crystal,” “meth,” or “speed,” as MA is variously called, can be injected, smoked, snorted, or ingested orally or anally. The timing and intensity of the “rush” that accompanies the use of MA, which is a result of the release of high levels of dopamine into the brain, depends in part on the method of administration. Specifically, the effect is almost instantaneous when smoked or injected, while it takes approximately 5 minutes after snorting or 20 minutes after oral ingestion. Immediate physiological changes associated with the use of MA are similar to those produced by the fight-or-flight response and include increased blood pressure, body temperature, heart rate, and breathing rate. Negative side effects include high body temperature, stroke, cardiac arrhythmia, stomach cramps, and shaking, as well as increased anxiety, insomnia, aggressive tendencies, paranoia, and hallucinations (King & Ellinwood, 1997; Office of National Drug Control Policy, 1998; Rawson, 1998).

Prolonged use of MA may result in a tolerance for the drug and increased use at higher dosage levels, creating dependence. Such continual use of the drug with little or no sleep leads to an extremely irritable and paranoid state. Discontinuing use of MA often results in a state of depression, as well as fatigue, anergia, and some types of cognitive impairment that last anywhere from 2 days to several months (Simon et al., 2000).

Both short- and long-term health effects have also been documented. As noted, negative consequences of MA abuse range from anxiety and insomnia to convulsions, paranoia, and brain damage, but in addition to the many direct effects on MA users are the indirect impacts on individuals and society (King & Ellinwood, 1997; Office of National Drug Control Policy, 1998; Rawson, 1998). Children of MA abusers are at high risk of neglect and abuse, and pregnant women's use of MA can cause growth retardation, premature birth, and developmental disorders in neonates (Lucas, 1997). Finally, extensive evidence indicates that in many Western US cities, MA is used extensively by gay males and is frequently associated with high-risk sexual behavior, a major factor in the transmission of HIV (Frosch, Shoptaw, Huber, Rawson, & Ling, 1996; Gorman, Morgan, & Lambert, 1995; Shoptaw, Reback, & Freese, 2002). Within this particular group, effective treatment for MA dependence may be one of the most important strategies in reducing the spread of HIV and other associated communicable diseases (Shoptaw et al., 2002).

## 3. MA addiction: a brain disease

There is currently a rapidly emerging wealth of information from animal and human brain research that has led to remarkable changes in the way MA addiction is understood. Research efforts in these areas have provided an entirely new perspective on the impact of drug use on basic neurophysiological systems. The conceptualization of addiction as a “brain disease” (Leshner, 1997) is easily understood as the data on MA and its effect on the human brain are better understood. Although individuals initiate their use of MA for a variety of psychological and sociocultural reasons, once MA has been administered to the human brain, profound changes begin to occur (Rawson, 1998; Cho, 1990). These brain structure and brain chemistry changes influence the basic biological unit of brain functioning—the neuron. MA appears to damage the neuron in ways that are different than, and in some ways more severe than other drugs of abuse (Rawson, 1998; Mathias, 1996). However, while there are profound changes to dopamine and serotonin systems, many of the changes appear to be reversible. Studies involving rats, guinea pigs, cats, and nonhuman primates have shown that high dosages of MA lead to damage of neuron cell endings, though some regrowth may occur (Cho, 1990). Demonstrating the extent to which MA can affect an organism's capacity to recover from MA effects, positron emission tomography (PET) scans of a monkey's brain after 10 days of use showed that dopamine production was significantly reduced for an entire year and that full recovery was not realized until 2 years later (Melega et al., 1997). The key ingredients for the necessary neurophysiological/neurochemical “healing” are ample amounts of time (6–12 months) and abstinence from MA use. This knowledge is likely to be relevant to application on the design and funding for MA treatment.

Clearly there are many important unanswered questions that require intensive investigation. For example, there is a rudimentary understanding of the manner in which MA affects the brain, but for the successful development of treatments, more information is needed. Why does MA produce such dramatic paranoia and other profound psychotic symptomatology in some, but not all individuals? How are these symptoms similar or different from schizophrenia? Do some people become schizophrenic as a direct result of MA use? What neurobiological systems are involved in reversing the effects of MA? Does the disruption in cognitive function recover as the brain recovers?

## 4. What do we know about treatment of MA disorders?

In many of the communities where MA is the major drug problem, the staffs of treatment programs have

extensive experience treating individuals with alcohol and marijuana use disorders. However, treatment programs and personnel that have for decades delivered traditional 12-step-based alcoholism treatment are unprepared for the influx of MA users. Although some traditional treatment elements may be appropriate for MA users, many treatment staff report feeling unprepared to address many of the clinical challenges presented by these patients. Poor treatment engagement rates, high dropout rates, severe paranoia, high relapse rates, ongoing episodes of psychosis, severe craving and protracted dysphoria, and anhedonia are clinical challenges that are frequently far more problematic than is seen with standard treatment populations (Rawson, 1998). In many small communities it is unclear which agency other than the police is the agency with the proper skills and knowledge to address the needs of MA users.

#### 4.1. Information and training

Current information is available to provide new treatment programing options for clinicians faced with the challenge of treating MA users. The Center for Substance Abuse Treatment (CSAT) Treatment Improvement Protocol (TIP) #33, Treatment of Stimulant Abuse is a useful resource that presents a review of the existing knowledge about treatment effectiveness with stimulant users, including MA users (Rawson, 1998). In addition, this document provides educational information and practical, applied recommendations useful in treating MA users. The TIP has an appendix with handout materials that can be used in clinical exercises in treatment sessions. Although there is information available to guide clinicians in treating MA users, in many geographic areas affected by MA there is neither the expertise nor the resources to implement these new treatment strategies. For traditional alcoholism counselors whose clinical expertise is primarily based upon their personal history of alcoholism, the severe psychiatric symptomatology of MA users is frequently beyond their clinical experience.

Training for these staff may be part of the answer. However, it may be necessary to add clinical staff with more professional background and training in working with severely mentally ill patient populations to adequately meet the clinical challenges of this patient population. Several of the clinical problems frequently encountered when working with MA users that are often unfamiliar to counselors who have primarily alcoholism treatment experience are the issues of MA and sexual behavior, MA and weight gain, and MA and ongoing paranoia. As discussed in the CSAT TIP #33, these issues are clinically quite commonly encountered when treating MA users and treatment knowledge in these areas is very important. In addition, recent issues of the *Journal of Psychoactive Drugs* (Anglin & Rawson, 2000) and *Journal of Addictive Diseases* (Rawson, 2002) are compilations of articles with new data on the nature and treatment of MA-related problems.

## 5. Treating MA problems

MA dependence is a difficult disorder to treat. The following characterization of the clinical challenges of treating MA users is condensed from TIP #33 (Rawson, 1998). Withdrawal from MA dependence is characterized by a protracted anhedonia and dysphoria that is accompanied by severe craving for the drug. Craving frequently occurs in response to exposure to conditioned cues (stimuli present during past episodes of MA use and euphoria). Such cues evoke powerful craving for MA via classical conditioning principles. The likelihood of continued MA smoking or injecting appears to be, in part, related to the strength of the craving experienced from these craving-generating cues. The withdrawal dysphoria present in the context of ubiquitous MA availability and ubiquitous conditioned cues can produce a very pernicious dependence; indeed, inpatient hospitalization may be indicated to treat long-term MA dependence, at least in initial stages of detoxification. Medically managed inpatient care is expensive, however, and widespread MA abuse has appeared in impoverished populations with very limited access to such inpatient resources.

#### 5.1. Medications

Research efforts to develop medications to aid in the treatment of MA-related disorders are at a relatively early stage of development. Currently there are no medications that can quickly and safely reverse life threatening MA overdoses. Similarly, there are no medications that can reliably reduce the paranoia and psychotic symptoms that frequently contribute to episodes of dangerous and violent behavior associated with MA use. As clinicians will attest, it would be tremendously helpful to have medications that could help MA users recover more quickly from the effects of chronic use. Medication(s) that could reduce symptoms in the early days and weeks of recovery could be extremely valuable in promoting engagement and retention in behavioral and psychosocial treatments (Vocci, 1996).

The problem of relapse to MA use is a complex process. However, one important set of contributing factors is the unpleasant emotional and cognitive impairments that accompany the protracted abstinence syndrome for months after MA use is discontinued. Medications that could lessen the severity of these symptoms could be of tremendous value in providing more successful treatments. At present, there have been fewer than 10 placebo-controlled double-blind efficacy trials of potential MA pharmacotherapies (Elkashef, 2001). One of the limiting factors in rapidly evaluating medications for MA-related disorders is that there are relatively few experienced pharmacotherapy research groups in the Midwestern and Western geographical areas impacted by MA. The need to develop new research groups capable of conducting addiction pharmaco-

therapy groups west of the Mississippi River is a critical need to increase the pace of medication development.

In response to this need, the National Institute on Drug Abuse (NIDA) has recently established the Methamphetamine Clinical Trials Group (MCTG), a network designed to provide new clinical research teams and sites in geographic areas where MA use is a major public health problem (Rawson, 2001). This network (funded by NIDA) consists of sites in San Diego and Costa Mesa, CA, Honolulu, HI, Des Moines, IA and Kansas City, MO and a coordinating center at UCLA. Studies of promising pharmacotherapies will be moved into these sites for assessment in double-blind, placebo-controlled trials.

### 5.2. Psychosocial/behavioral treatments

NIDA and CSAT have both sponsored research to evaluate the efficacy of several behavioral and cognitive behavioral treatments for stimulant use disorders. NIDA has also produced several manuals that have been empirically tested with stimulant-using populations, including manuals for cognitive-behavioral therapy and contingency management. Although the NIDA materials have been developed and tested with cocaine and crack users, there is evidence to suggest that cocaine and MA users respond quite similarly to behavioral and cognitive-behavioral strategies (Huber et al., 1997; Rawson et al., 2000). At the present time, CBT and CM techniques have the strongest empirical support for application with stimulant users (Rawson et al., under review; Rawson et al., in press).

Currently, a CSAT-funded, seven-site evaluation of an outpatient approach (Matrix Model) across a varied group of treatment settings and with a range of MA-using populations is nearing completion (Anglin & Rawson, 2000). The Matrix Model is a manualized, 16-week, nonresidential, psychosocial approach used for the treatment of drug dependence for more than a decade (Rawson et al., 1995; Rawson, Huber, et al., 2002; Rawson, Obert, McCann, Smith, & Scheffey, 1989; Shoptaw, Rawson, McCann, & Obert, 1994). The foundation of the model relies on cognitive-behavioral principles and basic goals: (1) stop drug use; (2) learn issues critical to addiction and relapse; (3) receive education for family members affected by addiction and recovery; (4) become familiar with self-help programs; and (5) receive weekly monitoring by urine toxicology and breathalyzer alcohol testing. The Matrix Model is designed to integrate several interventions into a comprehensive approach. Elements of the program include individual psychotherapy, relapse prevention and family education groups, urine testing, and participation in 12-step programs. Content of the treatment program is tailored to individual needs, although basic program elements are structured and manualized. Previous results from a number of open trials using the Matrix approach have been published in the research literature (Huber et al., 1997; Rawson et al., 1995; Rawson, Huber, et al., 2002; Shoptaw et al., 1994).

Although these treatment development efforts have delivered several empirically supported treatment protocols, the success of these approaches leaves much room for improvement. Efforts to establish novel psychotherapy/behavioral treatments are essential, as are studies to determine how to modify existing protocols to more effectively address the needs of special populations. The recently initiated NIDA Clinical Trials Network will provide a valuable research vehicle for assessing new MA treatments and evaluating their application in real world community clinics (Hansen, Leshner, & Tai, 2002).

## 6. Limitations on current treatments

While training and development of knowledgeable clinical personnel are essential, they are insufficient if the funding necessary to deliver these treatment recommendations is not available. In many areas, the treatment system funding is divided into treatment for residential care (21 days–12 months), short-term detoxification (3–5 days), and generic, poorly structured outpatient treatments. Unfortunately, this combination of options frequently is not optimal for the needs of MA users. As described in TIP #33, intensive outpatient treatment is viewed as the primary treatment setting for MA users. While the optimal frequency and duration of treatment sessions are not well established, the consensus panel that produced the TIP suggests that 3–5 visits per week for the first several weeks may be necessary, with 2–3 sessions per week for at least 90 days, or probably longer. The extended treatment period for MA users appears to be of critical importance to allow treatment to be maintained through the most difficult period of protracted abstinence dysphoria, cognitive disruption, and anhedonia.

Treatment funding policies that promote short duration or nonintensive outpatient services are inappropriate for providing adequate treatment for MA users. One specific practice is a managed care practice of providing a maximum benefit of 20 outpatient sessions for the treatment of individuals with MA use disorders. As referenced in the research section above, MA use disorders involve profound changes in multiple areas of human brain chemistry and brain functioning. Brief superficial treatment benefits frequently promoted by managed substance abuse benefit policies are in direct opposition to what is known about the treatment needs of MA users. In areas where MA use is a significant presence, financing policies for the treatment of these patients should be made consistent with evidence about their treatment needs (Washton & Rawson, 1998).

## 7. MA users with special treatment needs

While intensive outpatient treatment protocols do appear to provide the primary treatment paradigm for most MA users, several groups require other treatment resources.

Those individuals who enter treatment with such severe psychiatric impairment that they are unable to safely function on an outpatient basis require admission and stabilization in a medically supervised treatment setting where short term use of antipsychotic and tranquilizer medications can be administered to reduce paranoia, psychosis, and agitation. The duration of treatment in this setting is variable. Many individuals require only 48–72 hours to resolve these debilitating psychiatric symptoms. Once these symptoms are resolved to allow the patient to be safely treated on an outpatient basis, transfer to this setting is appropriate. However, there are individuals whose psychiatric symptomatology is not quickly resolved. These patients require longer stays under medical/psychiatric supervision and may need ongoing treatment with antipsychotic medications.

Pregnant women and women with small children frequently require increased levels of care. While it may be possible to treat pregnant women in intensive outpatient treatment, attention must be given to monitoring and promoting proper prenatal care with these women while in treatment. In addition, it is important that clinical staff be capable of working with pregnant women who relapse in treatment. Frequently, there is an extreme lack of empathy exhibited by staff and other patients toward women who relapse during their pregnancy. Clinical staff who can properly address these treatment situations and effectively move these patients to more intensive levels of care when necessary is essential. Women with small children frequently require an increased level of support either via a women's and children's residential setting or an intensive day treatment setting with sober housing for women and children. The combined burdens of work, home care, childcare, and other family responsibilities, plus attending treatment frequently can induce such a level of exhaustion and fatigue that MA use may appear to be the only way to acquire sufficient energy to accomplish all of the responsibilities. Clearly under these circumstances, special treatment considerations are needed.

The needs of gay male MA users may require special treatment programming (Frosch et al., 1996). The use of MA by gay and bisexual men frequently becomes inextricably intertwined with their sexual and social behaviors. The unique and powerful nature of this conditioned pathology presents a clinical syndrome that often cannot be effectively discussed in mixed patient groups with heterosexuals. The importance of this issue and the difficulty of discussing it in mixed patient groups frequently results in very poor treatment engagement and early treatment dropout. The importance of successful treatment with this group is of particular importance as the sexual behavior of this group is a tremendously critical vector in the spread of HIV (Reback, 1997). The challenges of working with this patient group and strategies for improving treatment response has recently been described (Frosch et al., 1996).

Finally, as mentioned above under the criminal justice section, one common deterrent to successful treatment

efforts with MA users is their inability/unwillingness to recognize the problematic nature of their drug use. However one conceptualizes this problem, as “denial,” “ambivalence,” or “precontemplation stage of change,” the fact remains that many MA users are reluctant to enter treatment and once in treatment there is an unacceptably high early dropout rate. One very strong finding in the research literature is that stimulant users respond well to the effective use of contingency procedures (Higgins & Wong, 1998). Fortunately, this finding on the value of contingencies to effectively influence the behavior of stimulant users dovetails nicely with the very enthusiastic movement to use drug court strategies. Drug courts are based upon the rapid and certain application of contingent consequences based upon the behavior of the drug user. Drug court participants who successfully exhibit desired behaviors (e.g., treatment attendance and clean urinalyses) can earn their way to progressively less-demanding treatment requirements and ultimately to removal of legal sanctions. Those who are unable to produce the necessary desired behaviors are required to move to more intensive levels of care or enter periods of incarceration. The combination of the MA user ambivalence and the drug court movement appear to have a tremendous potential for synergy (Burden, Prendergast, Roll, & Rawson, 2001).

## **8. The treatment of MA use disorders in 2002: where do we stand?**

MA is a drug that has periodically produced problems in the US and is producing many severe public health problems in many parts of the world. Use of MA produces many of the same problems that result from cocaine, but there are some aspects of MA-related disorders that appear specific to consequences from MA. New information from brain imaging research has provided new perspectives on how MA use changes the neurochemistry of the brain and some understanding about the causes of the time course of symptom remission following discontinuation of MA use. Currently, psychosocial and behavioral treatments for MA have the best empirical support, while no pharmacotherapies exist that have demonstrated value for MA treatment. Large scale treatment development and evaluation programs sponsored by NIDA and CSAT offer promise to expand and improve the tools available to clinicians who deliver treatment services to MA users.

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